Soft Tissue Mass as Primary Manifestation of IgG4 Related Disease

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Abstract- IgG4- related disease is a systemic fibroinflammatory syndrome characterized by tumefactive enlargement of affected organ , diffuse lymphoplasma cells infiltration with a large number of IgG4 producing plasma cells and sclerotic changes. The most commonly involved organs are pancreas, lacrimal and salivary glands. Patients show good response to glucocorticoid therapy and despite its relapsing and remitting course, patients have good prognosis. We report an unusual presentation of IgG4- related disease manifested as isolated soft tissue mass of hand which is an extremely rare manifestation of this disorder.

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Introduction

Immunoglobulin G4 related disease (IgG4- RD) is a, relatively rare multisystemic fibroinflammatory, immune mediated disorder of unknown etiology (1-6). The disease is characterized by organomegaly and mass like lesions. The masses are mostly inflammatory composed of lymphoplasmacytic infiltration of many IgG4 producing plasma cells and sclerosis (3,7). The variable manifestations of IgG4- RD mimic many neoplastic, inflammatory and infectious diseases, with a wide spectrum of differential diagnoses (8). Elevated Serum levels of IgG4 is seen in most but not all of the patients (6,9-12). IgG4- RD can affect any organ in the body (2,3,6,7) and the most commonly affected organ is the pancreas (1,7). The lacrimal glands, bile ducts, retroperitoneum, kidney and salivary glands are other common affected organs (1-3,6).

Patients mostly suffer from multiple organ involvement, however, single organ involvement may also be seen (3,11).

IgG4- RD is more common in males than in females and usually affect middle aged, elderly patients (2,6,10,11). Epidemiology of IgG4- RD is not well known, so the prevalence of this disease is probably underestimated (3,6,7,13). usually the disease responses well to corticosteroid therapy but relapse is not uncommon (2,3,6).

Here we report an extremely rare case of an IgG4- RD presented by an isolated soft tissue mass of hand.

Case Report

The patient was a 42-year-old woman who suffered from a gradually enlarging swelling of dorsal aspect of left hand at 5th metacarpo-pharyngeal region, for 8 months. Physical examination revealed a soft tissue mass at that area. Sonography showed a hypoechoic solid soft

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tissue mass measuring 2.5 cm in diameter with two ecogenic foci measuring 1.5 and 2 mm located at posteromedial aspect of the 5th metacarpal bone.
The patient had no significant medical history. Complete imaging studies of thorax, abdomen and pelvic organs were unremarkable. Complete blood count, coagulative tests, liver and kidney function tests, CRP, ESR, CEA and CA19-9 were in normal limits . Her laboratory autoimmune workup including RF, anti CCP, C-ANCA, P-ANCA came back as negative .Serum IgG4 level was within normal limits.

The patient went under operation for surgical removal of the lesion and a Firm soft tissue mass measuring 2.5 cm was excised from the mentioned anatomical region.
The specimen was received at the pathology department. The excised mass was well defined and firm measured 2×1.5×0.9 cm (Figure 1).

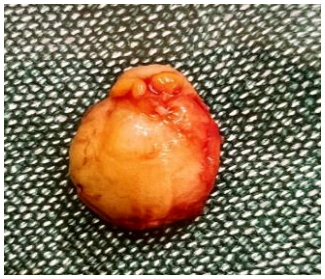

Figure 1. Gross appearance of the mass showing grayish- tan solid mass

On cut sections, homogenous tan surface was identified. Microscopically, Hematoxyline – Eosin (H&E) staining of 4 µ.m thick section showed well demarcated lesion composed of bland looking spindle shaped myofibroblastic cells arranged in fascicles, whorl and storiform pattern. Extensive infiltration of lymphocytes and plasma cells are also seen .There was no obliterative phlebitis (Figure 2).

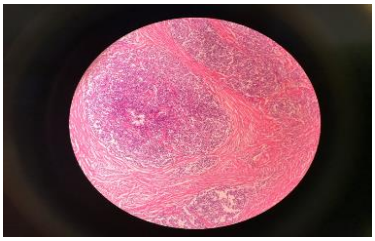

Figure 2. Histopathologic Finding of the mass showing severe fibrosis and aggregates of lymphocytes and plasma cells (×100)

IHC staining for HMB-45, Melan-A, synaptophysin, chromogranin were negative. CD138 was positive in plasma cells. Most of the CD138 positive cells showed positivity for IgG and more than 50% of IgG positive cells, revealed positivity for IgG4 (Figure 3).

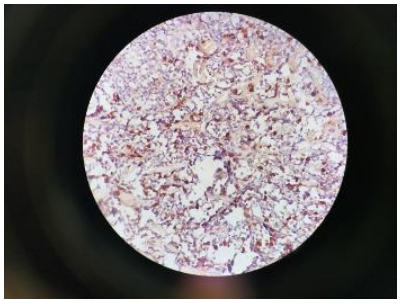

Figure 3. Immunohistochemistry findings: IgG positive plasma cells (×100)

The mentioned histopathological characteristics and IHC findings were consistent with the diagnosis of IgG4 related sclerosing disease.

Though, systemic evaluation showed no involvement of any other organs at the time of diagnosis and after 6 months follow up, however, the patient advised for regular follow-up to early detection of probable multiorgan involvement.

Discussion

IgG4-RD is a systemic disorder (6,9). The principal symptoms of IgG4- RD are slowly growing masses or enlargement of involved organs, sometimes resembling malignancy (9,14). Similarly, our patient suffered from gradually enlargement of a mass in her hand. The most common manifestation of IgG4-RD is autoimmune pancreatitis but many other organs may be involved (7). IgG4-RD is mainly a multiorgan disease (11,15). In about 60% of patients, involvement of more than one organ is evident at the time of diagnosis (15). Some patients have the disease restricted to only one single organ for many years and multiorgan disease might appear months or years later (11,15,16). So, Whole body evaluation of patients presenting with single organ disease is necessary, to prevent substantial organ damages due to fibroinflammatory nature of the disease (15). Although rare, similar to our case, IgG4- RD can be presented as an isolated soft tissue mass (7,9). In addition, presentation of soft tissue mass related to IgG4-RD in the limb, similar to our case is extremely rare (7). The previously reported cases were in subcutaneous adipose tissue, thoracic paravertebral space and extra-ocular muscles (7).

According to the Japan college of Rheumatology, diagnostic criteria for IgG4-RD are as follow:1) serum IgG4 Level> 135 mg/dl, 2) diffuse or localized enlargement or mass formation of involved organ, 3)

histopathologic findings of tissue fibrosis, and significant infiltration of lympho- plasma cells with more than ten IgG4- positive plasma cells per HPF 4) $IgG4^+$ plasma cells/IgG^+ plasma cells ratio more than 40%, and 5) storiform fibrosis (2,7,8). It should be noted that elevated serum level of IgG4 is the main feature of the disease, but it is not strictly confined to this diagnosis, because increased levels of serum IgG4 may also occur in many other diseases such as Castleman disease, Rasai-Dorfman disease and inflammatory bowel disease (7,10,14).

On the other hand, elevated serum level of IgG4 is found in most but not all patients (16,17). In fact, patients with more than 2 involved organs, usually have high serum levels of IgG4 (15), but most patients with isolated form of IgG4- RD usually do not have marked increase in serum IgG4 level (3).

Histopathological evaluation of the affected organ plays a crucial role in definitive diagnosis (7,12,15). Histopathologically, IgG4- RD is diagnosed by tissue infiltration of lymphocytes and IgG4 positive plasma cells with accompanying sclerosis and phlebitis (9-12,17). Some histopathologic variations are seen among different involved organs, for example phlebitis, as one of the common histologic findings, is very common in pancreas and submandibular salivary gland but is rarely seen in other organs such as lacrimal glands (7,9-11).

IgG4-RD mostly affects men above 50 years of age (2,5,7,11). But our patient was a 42-year-old female. Characteristically, IgG4- RD has a good therapeutic response to glucocorticoid by improvement of organ function and symptoms and reduction the size of the mass (1,7,9). In cases resistant to glucocorticoid therapy, other medications such as azathioprine, mofetil myophenolate, and rituximab have been used as second line of treatment (7,9,10). As IgG4- RD is almost a recently recognized disease, the natural history and prognosis is not well described, however, despite the good response to glucocorticoid, disease relapse and organ dysfunction due to fibroinflammatory changes can be seen (6,9). Additionally, the possible risk of malignancy is not clear, yet (9,14).

Despite its rarity, IgG4- RD should be considered as a differential diagnosis in soft tissue masses, especially when there is fibroinflammatory changes, in order to avoid misdiagnosis and irrelevant treatment which can result in irreversible fibrotic changes in the involved organ . Systemic evaluation and follow-up of the patients even with involvement of only single organ is necessary, because some of these patients may progress to multiorgan involvement over months or years.

The study is approved by the ethic committee of the Urmia University of Medical Sciences, Urmia, Iran (Ethics No. IR.UMSU.HIMAm.REC.1402.151).

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